

## REMARKS

In the Office Action of January 13, 2010, claims 1-2, 6-7, 23-24, 26-27 and 29-39 stand rejected. Claims 1-2, 6-7, 23-24, 26-27, 33 and 38-39 have been amended to recite, "hematopoietic stem cells" and find support throughout the specification, such as in the abstract. Claims 2, 7, 24 and 27 have been amended to recite "CD34+ cells" and find support throughout the specification, such as in the section labeled "Ongoing studies in human hematopoietic stem cells", Figure 11 and Figure 15. Claim 39 has been amended to correct matters of form. Claims 29-32 and 34-37 have been canceled. Claims 3-5, 8-22, 25 and 28 were previously canceled. New claims 40-43 have been added and find support throughout the specification, such as in the abstract, in the section labeled "Ongoing studies in human hematopoietic stem cells", Figure 11 and Figure 15. Thus, claims 1-2, 6-7, 23-24, 26-27, 33 and 38-43 are pending in the Subject Application.

Applicants respectfully submit that no new matter has been introduced by the amendments to the claims and addition of new claims.

### A) Priority

The Subject Application is a national stage entry under 35 U.S.C. § 371 of international application PCT/US2004/35220, which claims priority under 35 U.S.C. § 119(e) to U.S. provisional applications 60/514,329 filed October 24, 2003 and 60/620,154 filed October 19, 2004. The Examiner asserts that provisional application 60/514,329 fails to provide adequate support or enablement for one or more of the claims of the Subject Application. Specifically, the Examiner asserts that provisional

application 60/514,329 fails to provide support for the method of delivering small RNA interfering sequences (siRNA) to stem cells for the reduction of p18 levels in the intracellular environment of the stem cells. Applicants agree and note that the claimed method of delivering siRNA to stem cells is supported in provisional application 60/620,154 filed on October 19, 2004 (See Amendment to Specification, Response to Office Action filed January 23, 2009, page 3).

**B) Rejection of Claims 1-2, 6-7, 23-24, 26-27, 30, 32-33, 35 and 37-39 under 35**

**U.S.C. §112, first paragraph**

Claims 1-2, 6-7, 23-24, 26-27, 30, 32-33, 35 and 37-39 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Examiner asserts that the specification is not found to be enabling for promoting/stimulating self-renewal of a population of any stem cells by reducing intracellular levels of p18 through use of siRNA sequences (Office Action, page 5). Applicants respectfully disagree. However, in order to expedite prosecution of this matter, claims 1-2, 6-7, 23-24, 26-27, 33 and 38-39 have been amended to recite, "hematopoietic stem cells". In addition, claims 30, 32, 35 and 37 have been canceled.

Thus, Applicants submit that sufficient enablement has been provided by the amendment to claims 1-2, 6-7, 23-24, 26-27, 33 and 38-39. Accordingly, withdrawal of the rejection of claims 1-2, 6-7, 23-24, 26-27, 30, 32-33, 35 and 37-39 under 35 U.S.C. §112, first paragraph is respectfully requested.

**C) Rejection of Claim 39 under 35 U.S.C. §112, second paragraph**

Claim 39 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Specifically, the Examiner asserts that it is unclear if claim 39 is intended to depend from a previous claim or if it is intended to be an independent claim (Office Action, page 9).

Applicants submit that claim 39 was intended to be an independent claim. Thus, claim 39 has been amended to independent form. Accordingly, withdrawal of the rejection of claim 39 under 35 U.S.C. §112, second paragraph, is respectfully requested.

**D) Rejection of Claims 1-2, 6-7, 23-24, 26-27, 29, 31, 33-34, 36 and 38-39 under 35 U.S.C. §103(a)**

Claims 1-2, 6-7, 23-24, 26-27, 29, 31, 33-34, 36 and 38-39 stand rejected under 35 U.S.C. § 103(a) for assertedly being obvious in view of Yuan *et al.*, Nature Cell Biology, May 2004, Vol. 6(5), pgs. 436-442 (hereinafter, "Nature paper") in view of U.S. Patent No. 6,033,847 to Sherr *et al.* (hereinafter "Sherr") further in view of U.S. Patent No. 5,837,507 to Largman *et al.* further in view of Bertrand, J.R., "Comparison of antisense oligonucleotide and siRNAs in cell culture and in vivo", Biochemical and Biophysical Research Communications, 2002, 296: pages 1000-1004 (hereinafter, "Bertrand") further in view of An, D.S., "Efficient lentiviral vectors for short hairpin RNA delivery into human cells", Human Gene Therapy, 2003, 14: pages 1207-1212

(hereinafter, "An") further in view of Walters, D.K., "The effectiveness of double-stranded short inhibitory RNAs (siRNAs) may depend on the method of transfection", Antisense and Nucleic Acid Drug Development, 2002, 12: pages 411-418 (hereinafter, "Walters"). Applicants traverse this rejection for at least the reasons set forth herein.

As set forth herein, pending claims 1-2, 6-7, 23-24, 26-27, 33 and 38-39 are supported by provisional application 60/620,154 filed on October 19, 2004. The primary reference, "Nature paper", was published on May 1, 2004. Thus, Applicants submit that the Nature paper was published less than 1 year before the filing date of provisional application 60/620,154. Applicants submit that MPEP § 2132.01 states:

[a]pplicant's disclosure of his or her own work within the year before the application filing date cannot be used against him or her under 35 U.S.C. 102(a).

In addition, the current inventive entity of the Subject Application and provisional application 60/620,154 includes Tao Cheng. In contrast, the Nature paper includes the following authors: Tao Cheng, Youzhong Yuan, Hongmei Shen, David S. Franklin, and David T. Scadden. Applicants submit that MPEP § 2132.01 states:

[w]here the applicant is one of the co-authors of a publication cited against his or her application, the publication may be removed as a reference by the filing of affidavits made out by the other authors establishing that the relevant portions of the publication originated with, or were obtained from, applicant.

-and-

[t]he 102(a) rejection can be overcome by adding the coauthors as inventors to the application if the requirements of 35 U.S.C. 116, third paragraph are met.

Applicants attach a declaration of David S. Franklin under 37 C.F.R. § 1.131. In the declaration, Dr. Franklin indicates his contribution to the Nature paper and also declares

that the conceptual portions related to the self-renewal of hematopoietic stem cells in the absence of p18 in the Nature paper originated with Tao Cheng, Youzhong Yuan, Hongmei Shen and David T. Scadden. Applicants also attach a petition to add inventors Youzhong Yuan, Hongmei Shen, David T. Scadden and Hui Yu to the Subject Application under 37 C.F.R. § 1.48(a).

Accordingly, Applicants submit that the Subject Application and the Nature paper are considered works of Tao Cheng, Youzhong Yuan, Hongmei Shen, and David T. Scadden. Applicants submit that since the Nature paper is their own work, it cannot be used as prior art to reject the pending claims of the Subject Application. Hence, Applicants request that the Nature paper be removed as a prior art reference.

With the removal of the Nature paper, Applicants submit that the U.S.C. § 103(a) rejection resembles the same exact U.S.C. § 103(a) rejection cited in the Office Action of July 31, 2009, which was previously overcome. This rejection includes the following prior art references: Sherr, Largman, Bertrand, An and Walters. For the same reasons as set forth in the record, Sherr provides no teaching or suggestion that would lead one of ordinary skill in the art to the Applicants' claimed method of promoting or stimulating self-renewal. This is further supported by the Examiner on page 11 of the present Office Action mailed January 13, 2010.

Furthermore, Largman provides no teaching that, when combined with Sherr that would lead one of ordinary skill in the art to the Applicants' claimed method of promoting or stimulating self-renewal. Indeed, the Examiner only cites Largman for its teachings of reintroducing hematopoietic stem cells into a human.

In addition, Bertrand provides no teaching that, when combined with Sherr and Largman that would lead one of ordinary skill in the art to the Applicants' claimed method for promoting or stimulating self-renewal. Indeed, the Examiner only cites Bertrand for its teachings that siRNA technology is effective for silencing gene expression in mammalian cells.

Furthermore, An provides no teaching that, when combined with Sherr, Largman, and Bertrand that would lead one of ordinary skill in the art to the Applicants' claimed method of promoting or stimulating self-renewal. Indeed, the Examiner only cites An for its teachings of delivering siRNA molecules to cells using lentiviral vectors.

In addition, Walters provides no teaching that, when combined with Sherr, Largman, Bertrand, and An that would lead one of ordinary skill in the art to the Applicants' claimed method of promoting or stimulating self-renewal. Indeed, the Examiner only cites Walters for its teachings of delivering siRNA molecules to cells using electroporation.

For at least the reasons set forth herein, Applicants submit that the combined teachings of Sherr, Largman, Bertrand, An and Walters do not establish a prima facie case for obviousness because one of ordinary skill in the art reviewing the combined teachings of the references would not be inclined to arrive at the claimed method of promoting or stimulating self-renewal comprising:

1. a population of human hematopoietic stem cells;
2. siRNA;
3. reduction of p18 levels.

In addition, claims 29, 31, 34 and 36 have been canceled

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 1-2, 6-7, 23-24, 26-27, 33 and 38-39 under 35 U.S.C. §103(a) in view of the Nature paper further in view of Sherr, Largman, Bertrand, An and Walters.

**E.) New Claims 40-43**

New claims 40-43 recite novel and non-obvious methods of promoting or stimulating self-renewal of a population of human hematopoietic stem cells by reducing intracellular levels of p18. The cited references, Sherr, Largman, Bertrand, An, and Walters do not teach or suggest those recited methods of promoting or stimulating self renewal.

Thus, Applicants believe that claims 40-43 are patentable in view of the cited prior art. Accordingly, consideration and allowance of new claims 40-43 is respectfully requested.

**CONCLUSION**

Applicants respectfully submit that claims 1-2, 6-7, 23-24, 26-27, 33 and 38-43 recite novel and non-obvious methods of promoting or stimulating self-renewal. Applicants believe that these claims define over the prior art of record and are in proper form for allowance. In view of the foregoing, Applicants respectfully submit that the Subject Application is in condition for allowance. Accordingly, reconsideration of the rejections and allowance of claims 1-2, 6-7, 23-24, 26-27, 33 and 38-43 at an early date are earnestly solicited.

Applicants do not otherwise concede, however, the correctness of the rejections with respect to any of the dependent claims not discussed above. Accordingly,

Applicants hereby reserve the right to make additional arguments as may be necessary to further distinguish the dependent claims from the cited references based on additional features contained in the dependent claims that were not discussed above. A detailed discussion of these differences is believed to be unnecessary at this time in view of the differences in the claims discussed herein.

Applicants further submit that canceled claims 3-5, 8-22, 25, 28-32 and 34-37 may be filed in a subsequent continuation application.

If the undersigned can be of assistance to the Examiner in addressing any additional issues to advance the application to a condition of allowance, please contact the undersigned at the number set forth below.

Respectfully submitted,

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Date

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